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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/288,344	04/08/99	SEIDMAN E	P-PM-3474

HM12/0804

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EXAMINER	
CRANE, L	
ART UNIT	**PAPER NUMBER**
1623	4

DATE MAILED: 08/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/288,344	~~Xxxx~~ Seidman et al.
Examiner	**Group Art Unit**
L. E. Crane	1623

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ---3---- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 04/08/99 (application papers).

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-34 ---------- is/are pending in the application.

Of the above claim(s) ---------- is/are withdrawn from consideration.

☐ Claim(s) ---------- is/are allowed.

☒ Claim(s) 1-34 ---------- is/are rejected.

☐ Claim(s) ---------- is/are objected to.

☐ Claim(s) ---------- are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on ---------- is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on ---------- is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d) Claim of domestic priority is acknowledged. 7

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) ----------.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: ----------.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). ----------

☒ Notice of Reference(s) Cited, PTO-892

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other ----------

Office Action Summary

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

No claims have been cancelled and no preliminary amendments filed as of the date of the instant Office action.

Claims **1-34** remain in the case.

Claims **1-34** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1**, line 2, the term "6-mercaptopurine drug treatment" contains a superfluous term ("drug") which may be deleted without changing the meaning of the term or the claim. This same problem reoccurs in claims **7, 19 and 30**.

In claim **1**, line 4, the term "a 6-mercaptopurine drug" contains a superfluous terms ("a" and "drug") which may be deleted without changing the meaning of the term or the claim. This same problem reoccurs in claims **7, 19 and 30**.

In claim **1**, line 13, the term "6-mercaptopurine drug" contains a superfluous term ("drug") which may be deleted without changing the meaning of the term or the claim. This same problem reoccurs in claims **7, 19** (all four occurrences) **and 30**, and in claim **7**, line 2; claim **13**, line 2; and claim **29**, line 2.

In claim **4**, lines 3-6, various disease conditions are listed one of which "autoimmune enteropathy" appears to be synonymous with IBD or included within the scope of IBD/Crohn's Disease. It is also unclear what the relationship of the remaining 5 disease conditions enumerated are to IBD and/or Crohn's disease Applicant is respectfully requested to explain each of the noted term's distinction from IBD and/or Crohn's disease. This same problem reoccurs in claims **10 and 22.**

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1-34** are rejected under 35 U.S.C. §103(a) as being unpatentable over Sandborn (PTO-892 ref. **R**) in view of Sandborn **'915** and further in view of Berkow et al. (PTO-892 ref. T).

The Sandborn reference is a review article which describes the medicinal activity of azathioprine(AZA)/6-mercaptopurine (6-MP) in the treatment of Crohn's Disease, inflammatory bowel disease (IBD), ulcerative colitis and related conditions. At column 1 at page 93 this reference makes reference to a Mayo clinic study which determined that genetic factors make some hosts particularly sensitive to blood levels of the noted active ingredients in view of a low level of requisite enzymatic activity required to produce the active

metabolite(s) in vivo. At p. 95 this reference discloses toxic effects of AZA/6-MP administration at the second full paragraph of column 1 noting pancreatitis, allergic reactions and drug hepatitis among others. Leukopenia is noted in the third full paragraph.

Sandborn **'915** is directed to the treatment of Crohn's Disease by administration of azathioprine and 6-mercaptopurine and further specifies ranges for blood cell concentrations of 6-thioguanine and 6-methylmercaptopurine, which concentration are taught to be determinable in the disclosure at column 9, line 1 to column 10, line 11. See in particular column 9, lines 53-55 et seq and column 10, lines 4-6 et seq.

Berkow et al. discloses at pages 833-834 under the heading "Immunosuppressive drugs" that azothioprine and 6-mercaptopurine are effective in the treatment of Crohn's Disease, but indicates that side effects including pancreatitis and leukopenia (drug-induced blood cell depletion) are indicia of excessive immunosuppressive drug concentrations and must be avoided.

Disclosure in the prior art of the administration of AZA and/or 6-MP to treat Crohn's Disease and/or IBD and related disease conditions (Sandborn, Sandborn '915 and Berkow) when combined with specific teachings in Sandborn '915 of how to use high performance liquid chromatography (HPLC) to determine drug levels, including drug levels in blood cells, and teachings of side effects to be avoided and the reasons for their occurrence in Sandborn provides the ordinary practitioner with all of the elements of the instant disclosed invention and appears to leave no definable subject matter which has patentable distinction in view of the noted art. The election of generic testing protocols within the instant claims are

deemed to be nothing more than a description of how the information of the prior art would guide the careful practitioner in the administration of AZA/6-MP to a Crohn's Disease patient, and possibly in particular to a Crohn's Disease patient suffering from genetic limitations which limit the rate of sub-toxic AZA/6-MP administration. For these reasons, no claim has been found to contain patentable subject matter.

Therefore, the instant claimed improvement in the treatment of immune-mediated gastrointestinal disorders including IBD/Crohn's Disease by the monitoring of the administration of 6-mercaptopurine or its prodrug azathioprine (chemical structure provided in PTO-892 ref. S) in order to avoid toxic effects on the blood or the liver of the host being treated would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

References made of record but not cited above are deemed to be either equivalents to the cited references or to be of interest as closely related prior art which shows the state of the relevant prior art.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are **(703) 308-4556** and **703-305-3592** .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L.

E. Crane whose telephone number is 703-**308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor can be reached at (703)-308-1235.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-**308-1235**.

LECrane:lec
8/2/99

L. Eric Crane
Patent Examiner
Group 1600